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GEORGE E. SHAMBAUGH, JR., M.D., *President*

JOSEPH W. HAMPSEY, M.D., *Secretary*

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ALLERGY IN OTOLARYNGOLOGY: HISTORICAL REVIEW

FRENCH K. HANSEL, M.D.
ST. LOUIS, MO.

AMONG the various manifestations of allergy, bronchial asthma was the first to be recognized as a definite clinical entity. It has been known since ancient times and is even mentioned in the Bible.

The modern period of clinical allergy began with the description of hay fever by Bostock[8,9] in 1819. Later John Elliotson[17] in England first suggested that hay fever is caused by the pollen of grasses. He also pointed out that nasal symptoms and asthma may be caused by animal emanations. For our present knowledge of hay fever, we are indebted to Blackley,[6,7] who, in 1873, performed the first skin tests for sensitivity to grasses. In this country, Morrill Wyman[66] in 1872 was the first to recognize ragweed as a cause of hay fever. In 1903 Dunbar[15] repeated Blackley's experiments and introduced modern immunologic methods for the diagnosis and treatment of hay fever. Noon[40] of London, however, was the first to introduce the therapy calling for the injection of pollen extracts, following the preseasonal plan of beginning with small doses and gradually increasing them to maximum tolerance.

The most outstanding among the early observations were those of Henry Hyde Salter,[50] who in 1864 published a treatise "On Asthma; Its Pathology and Treatment." He first described the cells in the sputum, which were later in 1879 designated by Ehrlich[16] as eosinophils. Among the causes of asthma he mentioned food, drink, and smoke. He was the first to describe asthma caused by animal emanations. Salter himself was sensitive to cat dander and he gave a vivid description of his own case history. He noted reactions in the eyes and on the lips and cheeks from direct contact with cat dander. He described the positive skin reaction which resulted from the scratch of a cat's claw.

In 1871 Leyden[36] and also Charcot found small oblong octahedral crystals in the sputum of asthmatics. In 1882 Curschmann[14] described the spirals which are designated by his name.

In 1871 Voltolini cured a patient of bronchial asthma by the removal of a nasal polyp. This was probably the beginning of nasal surgery in allergic patients.

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Anaphylaxis

Intimately associated with the evolution of antitoxin came the discovery of anaphylaxis and its explanation. The original observations on this subject were contributed by Richet[48] and his associates (1898-1902). In 1903 Arthus[1] described the phenomenon designated by his name. Further outstanding observations on anaphylaxis were made by Rosenau and Anderson[49] in the United States in 1906 and by Otto[41,42] (1906-1907) in Germany. In 1906 von Pirquet[44] introduced the term "allergy" to designate these reactions which occur in man.

Weichardt[61] in 1905 and Wolff-Eisner[64] in 1906 were the first to suggest that hay fever may be an anaphylactic phenomenon. After Auer and Lewis[2] in 1910 described the outstanding pathologic picture of anaphylactic shock in guinea pigs as that of bronchospasm, Meltzer[37] (1910) suggested that by analogy bronchial asthma might be an anaphylactic disease. In the meantime, Noon (1911) was making his observations on the treatment of hay fever, as already mentioned. These observations of anaphylaxis in animals and clinical observations on hay fever and asthma mark the beginning of clinical allergy as practiced up to the present time.

Allergy of the Nose and Paranasal Sinuses

The early observers in otolaryngology made a distinction between the so-called catarrhal and the suppurative diseases. The catarrhal diseases were chiefly those we recognize today as allergic. In Bosworth's text on diseases of the nose and throat,[10] published in 1896, he devotes 11 chapters, or about a hundred pages, to the discussion of the catarrhal diseases but covers the subject of the accessory sinuses, excluding surgical procedures, in 25 pages.

The diagnosis of the nasal conditions was based upon the symptomatology and the gross pathologic findings. The x-ray was not as yet available at that time, but the finding of eosinophils in the secretions and the demonstration of edema and eosinophilic infiltration of the tissues in thickened membranes of the sinuses and the polyps were reported in the German otolaryngologic literature about 10 years before this time. As will be pointed out later, these significant findings did not receive recognition until about 40 years later (1927). The classification, diagnosis and treatment of nasal

diseases as presented by Bosworth in 1896 were representative of the time from about 1875 to 1927. During this period of 50 years, therefore, very little, if any, change or progress was significant except the addition of roentgen and bacteriologic examinations.

Among the catarrhal diseases Bosworth described so-called hypertrophic rhinitis, as characterized by vasomotor disturbances causing nasal stuffiness and postnasal discharge. Deflections of the septum and mulberry hypertrophy of the posterior tips of the inferior turbinates were contributing factors. He states that this condition may be associated with cough and asthma. Hypertrophic rhinitis is the counterpart of vasomotor rhinitis as known today. Most of these cases represent mild nasal allergies, but a small percentage are definitely not allergic. Bosworth also pointed out that dust, smoke, tobacco and various systemic diseases may play a part as etiologic factors, although the neurotic habit or tendency was considered of primary importance.

In another group of cases designated as nasal hydrorrhea the symptoms and pathologic changes correspond to typical nasal allergy. A great deal of emphasis was placed upon the importance of nasal reflexes arising from septal contacts, deviations or nasal polyps, often resulting in cough or bronchial asthma.

Early Contributions on Cytology and Pathology

Shortly after Ehrlich had named the eosinophil, Bizzozero,[5] in 1887, described Charcot-Leyden crystals in the nasal secretion and called attention to their possible relationship to the granules of eosinophils. Soon thereafter, Gollasch[20] (1889), Schmidt[52] (1891), Lewy[35] (1891), and Neusser[39] (1892) emphasized the presence of eosinophilic infiltration and edema of the tissues and the finding of eosinophils in nasal and bronchial secretions in cases of spasmodic coryza, nasal polyps and bronchial asthma. In 1895, Seifert and Kahn[53] in their atlas of pathology illustrated in color plates the edema and eosinophilic infiltration in nasal and sinus membranes and in nasal polyps in acute and chronic catarrhal rhinitis and sinusitis.

From the cases of nasal ganglion neuralgia, headaches and hyperplastic sphenoethmoiditis observed by Sluder[56] the pathologic study of the tissues removed was made by Jonathan Wright.[65] The primary interest in these specimens appeared to be directed to the bone changes and no attention was paid to the soft tissues. In 1928 we selected from the files (mostly Sluder's cases), 100 slides of tissue classified under hyperplastic sphenoethmoiditis and found that about 65 per cent showed the typical picture of allergy—edema and eosinophilic infiltration. In the introduction to Sluder's text, Wright did not mention these findings, but previously in 1898 he presented a detailed description of these changes noted in nasal polyps.

Nasal Allergy, Vasomotor or Hyperesthetic Rhinitis

The allergic nature of vasomotor or spasmodic coryza was first suggested by the French authors, Langlois[34] (1906), Billard[3] (1910) and Percepied[43] (1912). In this country Goodale[21] in 1916 was perhaps the first to confirm these reports. His original report concerned a group of 400 cases in which the etiologic factors were found to be animal emanations, foods and bacteria. Soon thereafter followed similar reports by Cooke[12] (1918), Selfridge[54] (1920), Walker[58] (1920), Turnbull[57] (1920), and Hansel[23] (1924). In 1921 Kern[28] and, in 1922, Cooke[13] called attention to the importance of house dust as well as animal emanations and foods as etiologic factors. These observations established nasal allergy as a definite clinical entity. Soon thereafter, numerous confirmatory reports appeared in the literature.

Allergy, Nasal Polyps and Sinusitis

Although nasal allergy was recognized about 1906, allergy as the cause of paranasal sinus disease did not receive recognition until about 20 years later. Then numerous reports appeared in the literature by such observers as Hansel[23,24] (1924, 1929), Finck[18] (1927), Mullin and Ball[38] (1928), Israel[27] (1928), Kistner[32,33] (1929, 1931), Weille[63] (1930), Coates[11] (1930), Kern and Schenck[30] (1933), Grove and Cooke[22] (1933), Walsh and Lindsay[60] (1934), followed by many others since then. The part played by bacteria in allergic sinusitis has been emphasized by Kistner (1929), Grove (1933) and Semenov[55] (1938). The significance of bacteria in allergy is still a moot question. Bacterial allergy has not been definitely proved. Bacteriologic investigations have not clearly distinguished between saprophytic and pure suppurative or pyogenic infection.

A very large percentage, but not all nasal polyps, are allergic. In 1934 Kern and Schenck[29] suggested the following classification of benign nasal polyps: (1) mucous polyps, edematous fibroma or myxoid fibroma; (2) mixed polypoid hyperplasia; and (3) papillary hypertrophy or mulberry polyp. Allergic polyps are included in group 2, but in some instances, as recently pointed out by Wallner,[59] papillary hypertrophy or mulberry polyps of the posterior tips of the inferior turbinates occurs with nasal allergy. Papillary or warty growths in the vestibule of the nose may occur with nasal

allergy but are rare. Their appearance on the lower edge of the inferior turbinate is not uncommon.

In discussing the relationship of allergy to nasal polyps Hirsch[26] in 1931 reviewed the literature on this subject and gave a very interesting survey of the various opinions expressed by the older observers as to the origin and significance of polyps and polypoid changes in the nose and paranasal sinuses. He began the survey with the report of Billroth[4] in 1855 and discussed in chronologic order the opinions of outstanding authorities up until 1927. Some observers believed that the edematous type of polyp originates primarily in the mucous membrane of the ethmoid surface, lining of the ethmoid cells and the surface of the middle turbinate, caused by infection or by catarrhal inflammation or a degenerative process. Disease of the ethmoid bone was thought to be an important cause. The extension of infection from the ethmoids and antrums was another theory, but we know today that in true sinus suppuration polyps are not common unless allergy has been followed by a pyogenic infection. Hirsch expressed the opinion that chronic catarrhal inflammation of the ethmoids and antrums was the cause of polypoid changes. Shortly after this period beginning about 1927, allergy became definitely established as the primary factor under consideration.

Roentgenographic Studies

With the development of the x-ray came an additional diagnostic procedure of great importance. The first roentgen examination of the sinuses was made by Scheier[51] in 1896. After the electric light became available, transillumination also came into use as a diagnostic procedure. The use of radiopaques began with the employment of aqueous mixtures of lead sulfate, reported by Weil[62] in 1903. Later bismuth was also used. A great improvement in technic came with the introduction of the halogenated oils by Forestier and Sicard[19] in 1922. Reverchon and Worms[47] (1925) were the first to use lipiodol in sinus diagnosis. About this time Proetz[45] reported his method for the introduction of lipiodol and other medicaments by displacement.

With the development of these roentgenographic methods of diagnosis, the literature soon became replete with reports on the relative efficiency of this procedure. Soon the x-ray became more evaluated as to its use and abuse. Many observers resorted to surgical procedures upon the sinuses almost entirely on the basis of the roentgen findings. Others, more conservative, used the x-ray only as an adjunct in diagnosis. In allergic cases one must be cognizant of the capriciousness of positive roentgen findings. As pointed out by Proetz,[45] acute allergic reactions may occur in the antrum, for example, giving rise to positive findings which may completely disappear within 24 to 48 hours, just as an urticarial wheal disappears from the skin. Furthermore, allergic edema of the sinuses may be reversible under allergic management. Conditions may be modified by acute or chronic infection and by irreversible changes.

One of the most comprehensive of the early reports was that of Kern and Schenck[31] in 1929. A study of 200 asthmatic patients and 50 normal controls was undertaken with the idea of determining the relative efficiency of the clinical and roentgenologic methods of diagnosis. Eighty-six of the asthmatic group were operated upon. Independent clinical and roentgen examinations of the sinuses in asthma showed an incidence of sinus disease of 80.5 per cent in the former and 67 per cent in the latter. There was considerable disagreement, however, between the findings of the two examinations in individual sinuses. It was concluded that positive roentgen ray findings do not imply clinically active disease, and that the clinical examination frequently overlooks chronic disease.

CORRELATION OF ALL FACTORS IN DIAGNOSIS AND TREATMENT

With the basic fundamentals which have been developed up to this time the diagnosis of nasal and sinus diseases can be established with a high degree of accuracy provided all of the following factors are properly correlated: (1) the history and symptoms, (2) gross pathologic changes, (3) the cytology of the secretions, (4) pathologic study of tissues, (5) bacteriologic and (6) roentgenographic examinations. Acute and chronic infections complicate the allergic picture. As a guide in diagnosis, cytology is one of the most valuable of all the various procedures. The common cold is the most frequent infectious complication and must be differentiated from the acute allergic exacerbation. Allergy and infections must be carefully evaluated in anticipated tonsillectomies.

OTHER MANIFESTATIONS OF ALLERGY IN OTOLARYNGOLOGY

So far, this discussion has been confined to the nose and paranasal sinuses, but there is hardly an anatomic structure in this entire field which may not be involved in the allergic processes. Briefly, they may be enumerated as follows: (1) the respiratory tract — nose, paranasal sinuses, adenoids and tonsils, nasopharynx, pharynx, larynx, trachea and bronchi; (2) the mouth — oral mucosa, gums, lips,

tongue, soft palate, and salivary glands; (3) the ear—auricle, canal, middle ear, eustachian tube, labyrinth and cochlea. A general survey of this over-all picture was presented at the Academy meeting in 1949 and appeared in the TRANSACTIONS for March-April 1950.

ALLERGY IN CHILDREN

It can not be too strongly emphasized that allergy more commonly begins in childhood and adolescence than in later life. About 50 per cent of cases of ragweed hay fever begin before the age of 15 years. Early respiratory allergy under the guise of frequent colds and bronchitis should be recognized. The removal of the tonsils and adenoids for the relief of such symptoms should not be recommended.

Recurring mumps in children suggests the possibility of allergy of the parotid gland. Deafness in children may be the result of eustachian tube involvement or serous otitis of allergic origin. Irradiation of the lymphoid tissue of the nasopharynx is rarely indicated in these cases.

On the whole, children respond most satisfactorily to allergic management and they should have the benefit of the medical service that is available to them.

ASSOCIATED MANIFESTATIONS OF ALLERGY OTHER THAN THOSE IN OTOLARYNGOLOGY

Other manifestations of allergy are not infrequently present and must be considered in the management of the patient, such as allergic bronchitis and bronchial asthma, gastrointestinal allergy, urogenital allergy, allergic headache and skin manifestations including urticaria, angioneurotic edema, eczema, purpura and contact dermatitis.

Finally, allergy must be considered as a complication of therapeutics. The introduction of the sulfonamides and, more recently, the antibiotics has resulted in reactions resembling serum sickness, which may manifest themselves as urticarial and angioneurotic edematous lesions in the field of otolaryngology. Other agents, such as a great variety of drugs, endocrine products, liver extract, insulin and other injectables, may produce the same types of reaction.

Although the fundamental principles of allergy as related to otolaryngology were known more than 50 years ago, definite progress has been evident only for the past 25 years, and especially the past 15 years. With the appearance of the text on "Allergy of the Nose and Paranasal Sinuses" and with the organization of the American Society of Ophthalmologic and Otolaryngologic Allergy in 1941 and the Hansel Foundation in 1947, a better dissemination of the developments of our knowledge of this subject has been possible. More than three hundred otolaryngologists are now affiliated with these organizations.

The members of the Society as a group have followed certain standard or uniform principles of diagnosis and treatment of otolaryngologic allergy. The small or low optimum dosage type of immunization, based in general upon serial solution titrations, has been adopted for the treatment of dust and pollen allergy. The results obtained by such methods have been reported by Black, Shambaugh, Hansel, Ashley, Rawlins, Craft, McGannon, Owen, House, Gill, Craddock, Stitt, Kuhn, Hampsey and others.

To those of us who have been interested in the development of allergy in our specialty, the progress being made previous to the founding of the above organizations was discouraging. The otolaryngologist was indifferent to allergy, perhaps because he was completely occupied with other types of work that he had always been doing. The treatment of infections was the most important problem in otolaryngology. With the advent of the sulfonamides and, more recently, the antibiotics, it is needless to mention the change that has taken place. As a result, the field of otolaryngology has become greatly limited and there has been considerable discussion recently about the problem of extending the specialty into other fields, especially those related to surgery.

With the inclusion of the practice of allergy in otolaryngology, this is entirely unnecessary. There is an unlimited amount of available material already existing in practice, and it is merely a question of being able to manage it.

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THE FUTURE OF ALLERGY IN OPHTHALMOLOGY AND OTOLARYNGOLOGY

M. MURRAY PESHKIN, M.D.
NEW YORK, N. Y.

IN any discussion of the future of allergy in ophthalmology and otolaryngology, it is necessary to consider not only certain problems which are the mutual concern of the three distinct specialties of ophthalmology, of otolaryngology and of allergy but also in what way each of these specialties will influence one another during the coming years. Allergy affecting the eyes and ears is of relatively low incidence and, therefore, is not as well known as the more common diseases of allergy affecting the upper and lower parts of the respiratory tract. For this reason a complete discussion of the interaction of these three specialties from the point of view of the allergist would be quite difficult to consider in detail. Here it would be simpler to state just in what way I believe the more common diseases of allergy affecting the respiratory tract will be of concern to the otolaryngologist and in what way similar phenomena will be part of the problem as allergic conditions of the eye and ear are studied. I accept with gravity and humility the invitation to prophesy the future of allergy in these specialties. I also wish to tell you how the allergist can lend encouragement and aid in the advancement of your current blueprint on the subject.

Time was when the allergic patient crossing the threshold of the office of an otolaryngologist was not only treated with medical procedures but also was offered surgical measures of therapy. In fact, the medical aspects were often only secondary. There were, primarily, many types of operations on the septum, the sinuses, polyps, adenoids, tonsils, turbinates, as well as other modalities applied to the nose, such as chemical and electrical therapy, which were even applied to the bronchial mucosa by means of the bronchoscope. Naturally these operative procedures with the physical modalities have undergone considerable evolution because of the newer understanding and influence of allergic phenomena in your specialty. With the passage of years, earlier claims had to be modified as the new knowledge of allergy and its relationship to these conditions accumulated. A position has finally been reached where it can be safely said that less surgery has been done than heretofore. This does not mean that the surgery of these conditions is neglected, as I shall point out shortly. It may be recalled that the clinical aspects of allergy really developed in the last 30 years. Indeed, some of you present have contributed to the subject. One might say, with the aid of a strange language spoken possibly by groups of somewhat bewildered aborigines from the state of "Allergiana," many of your patients hitherto mainly treated with surgical procedures were sometimes painlessly indoctrinated into the new cult of allergy. The elders from "Allergiana" were viewed with distrust at times and, indeed, justifiably suspected by the otolaryngologist when immunologic theory did not fit the clinical data for the results obtained.

It is quite obvious that there has been a certain amount of controversy between the otolaryngologist who persisted in the surgical point of view and the allergist who maintained that the immunologic framework was the primary cause and, therefore, was the proper therapeutic approach for the treatment of the patient. Out of this controversy has fortunately come a fusion of the two groups. Indeed, my appearance here is evidence of that fusion. Let me continue with another consideration. I have indicated that the surgical point of view was inadequate. Let me now state that perhaps some of my colleagues have with excessive zeal stressed the wedding march of the tuberculin syringe and the hypodermic needle as being the one and only method of handling what was apparently an immunologic problem. However, the concept held by the allergist, mainly imbedded in an immunologic structure, grew stronger as more of the antigen-antibody reactions were studied in detail. The allergists grew in number and the specialty as a whole prospered. Nevertheless, as with the surgery of the allergic patient, so did the tuberculin-syringe-and-hypodermic-needle route also lead to certain disappointments. The allergist then in turn became suspect because of the appreciable number of patients who failed to respond to treatment based upon his immunologic theory.

Otolaryngologists faced new developments in chemotherapy. Of significance is the way in which three groups of chemotherapeutic drugs

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entered the scene. The first group is the sulfonamide drugs, the second group the antibiotics, and the third group is the extracts of the adrenal glands and ACTH. Any consideration of the future of otolaryngology must include the way in which these new groups of drugs, developed within the last decade, will influence immunologic reactions notwithstanding the antihistamine drugs. For the endocrine group, an insufficient amount of data has been accumulated at this time to know just what the future will be. However, we do know that the antibiotics are decreasing the possibility of infections playing a major role in your specialty. A similar statement can be made for the sulfonamide drugs. Therefore, I state with a great degree of certainty that the role of infection in the allergic and potentially allergic patient will become decreasingly important.

I feel it necessary to emphasize that, for any group of people to survive, leadership must provide a plan for survival. It cannot be expected that every nose in the land would be subjected to plastic repair nor that every otolaryngologist desires to entertain the notion of adding a surgical procedure of that type to his therapeutic armamentarium. In view of all of the foregoing considerations, the otolaryngologist has to broaden his knowledge of medicine if he is to survive in his specialty. It is natural for me to remark that he should spread his wings to cover all phases of treatment which he is expected to administer. If he is to survive with dignity, he will be obliged to become a full specialist, a "compleat" otolaryngologist. In your ranks there is at least one colleague who pioneered with courage and wisdom. He sojourned in "Allergiana," struggled, sweated and toiled, and kept the faith. "Allergiana" today desires to repay its debt for the initial nourishment you gave it by acclaiming the return to your fold of a physician with a contagious sincerity who has served and continues to serve his fellow allergists and fellow otolaryngologists with unfaltering devotion and strength and honesty of purpose. His contributions to the literature are many and are a matter of record. He is deserving of the high esteem his colleagues hold for him. The physician is here tonight. His name is French K. Hansel. You are familiar with the Hansel Foundation at St. Louis, Mo., where otolaryngologists are taught allergy methods of investigation and of treatment. He founded the American Society of Ophthalmologic and Otolaryngologic Allergy, in which many of you are members. Here the language of allergy is sympathetically employed and the advances of the science of allergy as it affects your specialty are presented.

Keeping in mind what has been said, other thoughts on the future of allergy in ophthalmology and otolaryngology can now be further developed seriatim.

1. What is the minimum knowledge of allergy required of the ophthalmologist and otolaryngologist who desires to utilize allergy methods in his practice? To employ allergy methods, properly and intelligently, it is necessary to attune your minds to this less spectacular and nonsurgical field of medicine. Temperament, patience and aptitude play an important role in discharging your responsibility to the best interests of the allergic patient.

Allergy is the most common condition affecting the nose and paranasal sinuses. The relation of the nose to the bronchial tract is too well known for comment. The occurrence of asthma, a major disease, requires serious attention. For this reason, the otolaryngologist is obliged to treat both the bronchial and the nasal allergy. He is not expected to shuttle such a patient to an allergist for treatment of the asthma while he treats the nasal allergy. On the other hand, it would not make sense for the allergist to treat the asthma and refer the patient with an associated nasal allergy to the otolaryngologist for its specific treatment.

The ophthalmologist and otolaryngologist will be required to know the fundamental experiments underlying allergy and immunology and their clinical application. Such a basic course of instruction should cover not less than sixty hours. In addition, for at least two consecutive years a postgraduate course in allergy should be taken. Courses usually are from three to five full days long. At the same time it is essential to attend allergy clinics at least twice weekly for several years. Subscription to the national and international allergy journals and to reviews on allergy is important. Each specialist must consider and treat the allergic conditions found in his specialty as local manifestations of a systemic disturbance. The diagnosis and differential diagnosis of the various allergies and their effects on other tissues of the body is a responsibility you must assume. In short, you are to become a "compleat" specialist, the combined surgeon and internist.

2. The importance of attending an annual meeting of a national allergy society and attaining membership therein is obvious. It is also desirable to become a member of a local allergy society.

3. It is essential to create and maintain a close understanding between the ophthalmologist, the otolaryngologist and the allergist. On this basis a model of mutual assistance can be more easily implemented. The successful management of the complex and difficult respira-

tory allergies and their complications may require consultation with an allergist. The allergist will also have need of an authoritative evaluation by the ophthalmologist or by the otolaryngologist in certain cases.

4. "Bacterial allergy" of the respiratory system is a problem that requires further study despite progress in the field of antibiotic therapy. The immunologically trained otolaryngologist can add much knowledge to this moot question.

5. The role of the bronchoscope and its dangers when used to relieve asthma occurring at any age is a subject that requires further study and clarification. In certain cases of asthma, bronchoscopy is of importance in diagnosis and treatment. Here the otolaryngologist may render important help to the allergist.

6. The surgical approach in the treatment of allergy of the nose needs reappraisal. There is a need for more data and clarification on the effect of a standardized, expertly performed exenteration of the paranasal sinuses in cases with irreversible nasal pathologic change and its influence on a complicating asthma.

The immunologic and allergic aspects of otolaryngology have until relatively recent times been left to the allergist because the otolaryngologist had neither the feeling nor the inclination to become orientated in antigen-antibody reactions. Surgical methods of treatment were his primary interest. Gone is the day of advocating surgery for the treatment of seasonal and perennial allergic rhinitis. However, complications of these conditions do occur. A dark antrum is present and the allergist refers the patient to the otolaryngologist who, after irrigating the involved sinus, finds pus. Proper treatment clears up this intercurrent infection which, if allowed to run undetected, may mean chronicity and trouble for the patient.

Because the antrums and ethmoidal sinuses are the ones most frequently involved in allergy, involvement of the sphenoidal sinuses is too often overlooked in conservative and surgical treatment.

The otolaryngologist can help the allergist if the latter clearly recognizes the conditions requiring special nasal treatment. The patient with chronic or intractable asthma with irreversible nasal pathology may not respond to expertly administered specific allergy treatment. Here, immunization treatment alone cannot favorably alter the extensive perivascular infiltration and degeneration of the mucous membrane of the nose and paranasal sinuses. These tissues are a chronic source of focal infection. An intranasal operation for the complete exenteration of the diseased mucous membranes from the sinuses has proved extremely helpful in restoring the patient to function as a useful human being. Some of these patients no longer need immunization. In others, specific treatment must be continued, particularly with pollen antigens. It should be noted that one year after radical surgery the nasal mucous membranes are restored to normal texture and consistency. The operation is done not primarily to relieve asthma but rather to eliminate infection and irreversible processes. The age of the patients is usually 40 years or more with a history of asthma of ten years. Gross polyposis and troublesome infection requiring surgery are rare before the age of puberty. Hansel[4] stated that in the management of these cases general rules rather than specific ones must be adopted and that individualization of cases must be followed. In most instances, the pathologic process is one of a combination of allergic changes and secondary infection. Better teamwork can be expected to exist between allergy-conscious or allergy-trained otolaryngologists and rhinologically orientated allergists. As a consequence, it is believed that the incidence of irreversible pathology of the sinuses in allergic patients will in due time be considerably reduced.

The tonsils and adenoids. The allergically conscious otolaryngologist has an awareness that the mere presence of tonsils and adenoids per se is not an indication for their prompt removal. The surgical indications are too well known to be reiterated and are alike for allergic and nonallergic patients. For a small number of patients the removal of tonsils and adenoids may confer temporary relief from asthma for several months or more. For the remainder the asthma may become aggravated or be unchanged following surgery.

The allergist and the otolaryngologist must recognize that in some children following removal of tonsils and adenoids there occurs a rapid proliferation of the mucous membrane in Waldeyer's ring especially affecting the lateral and posterior walls of the pharynx. The tissue is a source of focal infection but its surgical removal is unsatisfactory and often contraindicated. The diseased tissue is most effectively eliminated with the application of radium.

What has been said about the allergic nose, throat and bronchi fundamentally applies to the ears and eyes. The allergy of the inner ears and eustachian tubes is usually secondary to nasal allergy. The allergic eye disorders, however, may be primary, the more common being perennial and vernal conjunctivitis, which is often regarded as a bacterial infection or strange disease despite the fact that every evidence points to a pollen etiology.

7. Psychodynamics in allergy. The role of psychologic disorders in patients with nasal[5] and bronchial allergy[2,3,6,7] has been stressed, especially in the last few years. As an allergist, Dr. Harold A. Abramson,[1] with the support and encouragement of the American College of Allergists, has blazed the trail. The otolaryngologist should absorb this important adjunctive procedure into his sphere of practice in order to understand the allergic patient better and to increase the incidence of improvement of or freedom from allergic disease.

8. It is well known that, spurred on by the allergists, some specialists in dermatology, pediatrics and internal medicine made notable contributions to the subject of allergy as related to their specialty. The sooner the otolaryngologist makes up his mind how far he wishes allergy to become part of his work, the sooner it can be determined what his minimum knowledge of allergy should be. Who is to teach allergy for the otolaryngologist? While it is desirable for the otolaryngologist to assume the major role in this training program, for the moment the number of otolaryngologists with immunologic learnings is inadequate to meet the demand. Thus, the teaching and training of necessity should be done largely by the allergist. Should the allergist be a subcertified allergist in internal medicine or a subcertified allergist in pediatrics, or both? After intensive study and training and extensive practice it can be prophesied that a number of otolarynglogists will drift into allergy more and more and eventually make it the major part of their practice. Such physicians, as allergists, will obviously greatly benefit the specialty of otolaryngology, as well as assume leadership in that phase.

Now anticipate with me for a moment, if you will, the irritation and ill will which will result when, ten years or more from today, the certified otolaryngologists who have become qualified instructors in allergy and have made important contributions to the literature and desire to be identified as otolaryngological allergists are informed that though they are allergists in fact, they can not be officially rated or certified as allergists. On the basis of precedents it is logical to assume that the otolaryngologists as well as the ophthalmologists will in due time clamor and be entitled to become subcertified allergists in their respective specialties. What, another subcertified allergist? Such a situation is confusing and, in fact, impractical and unrealistic. If anything, it is bound to retard the progress in the science of allergy and hence hasten the deterioration of the specialty of allergy to the ultimate detriment of the patient.

The need for an American Board of Allergy is obvious and of paramount importance if the subject of allergy is to be preserved in the best interests of the patient. With an American Board of Allergy within the framework of the Advisory Board of Medical Specialties, an ophthalmologist or otolaryngologist who qualifies as an allergist can, after meeting certain requirements, become a certified allergist. As a certified allergist he will be regarded with esteem and may practice allergy with dignity.

It has always been thought that a prophet is not recognized by his own people. Nevertheless, I have the strong feeling, since I am with colleagues, that my message will have more significance than that usually given a prophet by virtue of his own labors and achievements. For that reason my prophecies are really symbols of recognition of your own progress.

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THE DIAGNOSIS OF FOOD ALLERGY

THERON G. RANDOLPH, M.D.
CHICAGO, ILL.

THE clinical importance of the mechanisms of food allergy has become increasingly apparent since Rowe's pioneering contributions[30,31] in this field starting slightly over 20 years ago. As with all new basically important concepts in medicine, the profession passed through a stage of relatively slow acceptance of the fundamental role of food allergy in medical practice but, fortunately, we are now at a point in the curve of rapidly increasing recognition and application of these principles. Our position in this respect is due in no small part to the brilliant and clarifying clinical observations of Dr. Herbert J. Rinkel,[17,23,27] your guest of honor this evening.

Although my presentation deals primarily with the specific diagnostic measures employed in food sensitivity, I will attempt to inject a few preliminary remarks in respect to the incidence of food allergy and theoretic concepts concerning the mechanism of the food sensitization process.

Food allergy may be the sole or contributing cause of any of the so-called localized allergic manifestations. Of these the responses of the upper respiratory passages and orbital structures are so frequently encountered in practice that physicians sometimes find it monotonous in explaining the allergic origin of their patients' symptoms.

It should be emphasized, however, that in spite of the apparent localized effects of the allergic process, the entire body participates in it. In fact, food allergy frequently results in the production of constitutional symptoms including headaches of various descriptive types, weakness, fatigue, myalgia, arthralgia, as well as mental confusion, depression and sometimes episodes of psychotic behavior.[8,27] For example, in a recently studied case the experimental gavage of an allergenic food was shown on repeated occasions to result in the initial production of rhinitis and pruritus; these localized symptoms then subsided and were followed by the development of somnolence, mental confusion, dizziness, ataxia, and increasing degrees of muscular incoordination and hyperkinesis, finally reaching a stage characterized by amnesia, disorientation, regression and compulsive psychotic behavior requiring the use of physical restraints.[8] In other instances heretofore unreported, severe depressions have been induced experimentally following trial ingestion of allergenic foods and have been relieved following specific avoidance.

Although the mechanisms of food allergy have never been well understood, it is becoming increasingly clear that processes in addition to those concerned strictly with an immunity response are involved. I will attempt a brief discussion of some of these theoretical points.

One of the characteristics of the allergic reaction is the speed with which allergic symptoms develop in the highly sensitized individual on exposure to the specific allergen. In connection with food allergy it has been shown that the most rapidly absorbed physical forms of a food are the most highly allergenic as judged by the rapidity of onset and severity of symptoms following trial ingestion under the terms of the individual food test.[9,21] Under these circumstances it has been shown that spirits[10] and sugars[13,14,16] derived from a food produce more acute and immediate symptoms than occur from the ingestion of the more slowly absorbed forms derived from an identical source.

Increased tissue hydration is another characteristic feature of the allergic reaction as evidenced by microscopic examination of involved tissue as well as the gross aspects of allergic manifestations. The edema of the allergic reaction appears to be primarily intracellular in type in view of the relative absence of the features of dependency and pitting.

According to the acid-anoxia-endocrine theory of allergy recently developed by Clark and Randolph,[4] the intracellular edema of the food allergy reaction is believed to result from the fact that predominately acid end products of digestion accumulate within the cell more rapidly than they can be neutralized by the available buffering mechanisms. The resulting increased acidity of the cell sets in motion a rapidly occurring but closely integrated series of events. Extracellular fluid passes into the cell in association with altered permeability of the cell membranes and probable shifts in the relative concentration of intracellular and extracellular electrolytes, for it is well known

Associate in Medicine, Northwestern University Medical School.

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that proteins and other colloids absorb water when acidified.

If one may draw an analogy from the tissue changes occurring in experimentally induced localized allergic responses,[1,6] the apparent demand for increased extracellular fluid is presumably met by vasodilation and alterations in the permeability of the capillary walls. These changes, in addition to the presence of intravascular sludging of cellular elements, known to occur in at least certain allergic reactions,[33] are associated with a slowing of the peripheral circulation sufficient to interfere with the exchange of oxygen and carbon dioxide. The resulting tissue anoxia acts to accentuate both the cellular acidity and the edema, producing a vicious cycle of events. The body's first line of defense in combatting this rapidly developing acidification process within the cell is a shift of fluid from the extracellular to the intracellular compartments; this is undoubtedly associated with changes in the relative concentrations of electrolytes and perhaps significant changes in cellular enzyme systems.

As a second line of defense, eosinophils appear to be attracted from the slowed peripheral circulation, as shown by Kline, Cohen and Rudolph,[6] and it is quite possible that their alkaline granules may function to combat acidification of the tissues.

As a third line of defense in accordance with this theory,[4] the body calls upon the available alkali reserve for the direct neutralization of cellular acidity. There is suggestive evidence that the rapid exhaustion of these limited bicarbonate reserves serves to stimulate the adrenal cortex to activity[7]; this, in turn, presumably results in changes in the direction of alkalosis at the cell level inasmuch as the administration of exogenous ACTH is associated with the elaboration of alkaline cortical steroids.[32]

The beneficial effect of ACTH on the allergic reaction is now well established,[2,3,15,28] and in the absence of other feasible explanations, the mode of action of ACTH in bringing about temporary relief of allergic disturbances may be due to a shift in intracellular versus extracellular electrolytes in the over-all direction of alkalosis, reversing the direction of extracellular to intracellular fluid transfer which, according to theory, characterizes the allergic response.

According to this interpretation, an allergic reaction requires the existence of a specific sensitivity and an exposure to the food in question. Although one of these factors may be relatively greater than the other, allergic symptomatology presumably develops if the combination of the two exceeds the counterbalancing effect of the endocrine glands. This concept of allergic balance, modified from Vaughan,[35] is shown graphically in figure 1.

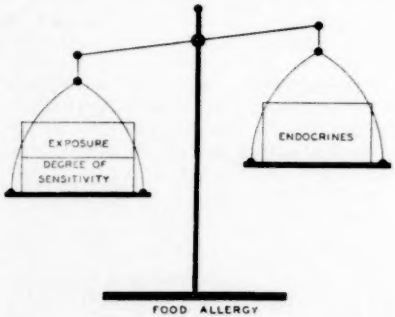

FIGURE 1.

The endocrine response is undoubtedly somewhat variable from time to time and quite possibly may afford more protection on one occasion than another, which might account for variations in the severity of allergic reactions following similar dietary exposures. The role of such a factor will necessarily remain somewhat speculative until the development of improved methods of measurement.

Much more is known in regard to the role of incidence of a food in the diet in respect to variations in the resulting clinical response in food allergy. In general, a patient is usually able to detect the presence of sensitivity to those articles of the diet eaten infrequently, or even to those foods usually taken regularly but which by chance are sometimes omitted for periods of four or five days.

Under such circumstances the individual usually develops an immediate allergic reaction which he ordinarily associates with the ingestion of the food in question. Although the statement is sometimes made that one can tell by a carefully recorded history whether or not food allergy exists as a cause of symptoms, this is true only in respect to those articles of the diet ingested occasionally. Patients are rarely ever able to detect the presence of a high grade sensitivity to corn, wheat, milk, eggs, potatoes or one of the sugars taken at least once daily.

The best explanation of the patient's failure to recognize the existence of sensitivity to major foods has been given by Rinkel[20,27] in his description of the masking effect produced by the ingestion of a specific food at a time when the individual is still in a reactive phase following the last ingestion of the same food. Under such circumstances one usually develops a transient and ordinarily undetected symptom

response which is followed by an amelioration of the previously existing chronic symptoms; this improvement persists for a variable number of hours and is then followed by a delayed accentuation of chronic symptomatology.

Although we are not able to interpret what is happening physiologically in this type of allergic response, it remains one of the most frequently encountered causes of chronic illness observed in the practice of medicine. In view of the incidence and importance of masked sensitivity, specific food allergy must be suspected on the basis of probability and proved or disproved by diagnostic measures which eliminate commonly ingested foods for at least four days and then permit their reintroduction to the diet under circumstances which favor the observation of their effects.

Any discussion of the diagnosis of food allergy presupposes that the existence of inhalant sensitivity has been carefully appraised and controlled by means of specific avoidance or adequate therapy prior to and during the course of diagnostic measures for the detection of specific food allergens. In this connection skin tests with inhalant extracts are highly reliable both quantitatively and qualitatively; in fact, their accuracy is of such a degree that specific treatment may be based directly upon determining the end-point of reaction in performing tests with serial dilutions.[12,24,25,26]

Unfortunately, a similar statement cannot be made for the reliability of skin tests with food extracts. Rowe,[29] Rinkel,[17] Vaughan,[34] Coca[5] and others interested in the diagnosis of specific food allergy by means of clinical ingestion technics have stressed the fallibility of skin tests with food allergens. The most careful statistical study of the accuracy of skin test technics has been made by Rinkel.[27] The writer believes that skin tests with food extracts in and by themselves are practically worthless and, inasmuch as both positive and negative "reactions" must be confirmed by ingestion technics, he has abandoned the use of skin test procedures in the diagnosis of specific food sensitivity.

The recommended approach in the specific diagnosis of food allergy is the performance of several individual food tests with the major articles of the diet based upon the probability of sensitization and the eating habits of the patient. The technic of this test, developed by Rinkel,[21,27] consists briefly in the absolute avoidance of a particular food for four days prior to its experimental ingestion under observation. The incidence and severity of symptoms are recorded per unit of time by an observer trained in the technic of the test for one half hour prior to the deliberate ingestion of the food in a fasting condition and for three half hour periods thereafter. A second feeding is given an hour after the first, providing an acute symptom response has not developed. The test is considered positive if there is a doubling or tripling in the incidence of coughing, sneezing or other symptoms found by experience to be associated with a positive reaction.[27]

Total leukocyte counts (enumerating double the number of leukocytes usually counted) are performed prior to the initial feeding and at 20, 40 and 60 minutes thereafter. In the absence of clear-cut reactive symptoms, some emphasis is given to the interpretation of the leukocyte responses, an empirical association of fairly high correlation having been shown to exist between the development of a leukopenia of 10 per cent or greater occurring in the postprandial blood observations and in the presence of delayed or cumulative types of food reaction.

This diagnostic approach is advantageous in that it permits the direct observation of the patient immediately prior to and during the course of induced allergic reactions. When applied to the first six or eight major allergenic foods in a patient's diet, the diagnostician learns something of the extent of involvement of the diet by the food allergy process. In the event of a narrow base of sensitivity, it is safe and expeditious to proceed with highly restricted diagnostic diets. If more than 50 per cent of the first group of foods is incriminated, one then proceeds with further individual food tests without placing this type of patient on a highly restricted diet.

It should be emphasized, however, that the patient experienced in this type of experimental testing can perform additional test procedures at home with a reasonable degree of accuracy. Furthermore, this diagnostic program can often be combined with the use of basic diagnostic diets.

The use of elimination diets of the type pioneered by Rowe[31] and particularly in the form currently employed (Rowe's cereal, milk, egg and fruit-free elimination diet) is a practical and useful diagnostic program. However, the use of any relatively fixed type of basic diet as the initial diagnostic program in food allergy presupposes that the selected list of permitted foods is relatively nonallergenic. Although this may be true for a majority of patients, the fact remains that any article of the diet is potentially allergenic and no food may be regarded as immune from causing allergic symptoms.

Coca's pulse rate technic[5] for the specific diagnosis of food allergy appears to be a workable program in the hands of those experienced in its use. It should be emphasized that

this is primarily a trial ingestion technic and the addition of the pulse measurements may, at least under certain circumstances, give clues of reaction not invariably obtained by other procedures.

One other diagnostic technic of value in selected cases, particularly in acutely ill hospitalized patients, is the institution of a fast of four to seven days' duration. This program is apt to free the individual from his chronic severe symptoms and, if so, impresses upon him the role of foods in this connection. The fast is broken by returning foods of relatively low probability of sensitization, one at a time every two or three hours, adding the more common allergens one at a time once or twice daily after caloric requirements have been met as a result of the earlier additions. Incriminated foods are avoided as they are detected. This program has been found advantageous in the specific allergic diagnosis of patients with mental syndromes of allergic origin in which it is difficult or impossible to secure sufficient cooperation of the patient to follow one of the above mentioned plans. As with many other standardized approaches in the diagnosis of specific food allergy, it is apt to break down to some extent when dealing with the patient who already has a widespread sensitivity at the time diagnosis is undertaken.

Once the individual has been freed of allergic symptoms on some type of diagnostic plan, the next stage is to return the previously omitted foods one by one in such a timing as to note most effectively the relationship of the added foods to the production of symptoms. The evidence obtained may be confirmatory of points in the history, the results of earlier individual food tests or other types of specific evidence. If the response upon reintroduction of a particular food to the diet is at all equivocal, it should be omitted again and subsequently returned to the diet in cumulative doses.

At this point the specific diagnosis of food allergy borders closely on the treatment of the food sensitization process, a point outside the scope of this presentation. As a matter of fact, it is impossible to separate these two aspects completely, for one should keep in mind fundamental principles of prophylaxis throughout the period of diagnosis and one ordinarily has to redeploy diagnostic procedures at various times in a predominately therapeutic phase of management of food allergy. An example of the first is the instruction of the wheat-sensitive patient in how to use corn and other cereal grains so as to minimize the danger of sensitivity spreading to other grains when wheat is eliminated; this is best accomplished by instructing the patient in rotating the use of a wide variety of substitutes. An example of the latter is the continual inquiry of the diagnosed patient in respect to the possibility that he may have developed a spread of sensitivity to a once tolerated article of the diet.

Regardless of the mode of diagnosis selected, it is imperative that the clinician attempting to diagnose specific food sensitivity control his patient's inhalant symptoms coincidentally as he carries out the diagnostic program. Another fundamental requirement is the obvious need of knowing the sources of the common food allergens in order that the individual may be enabled to avoid a particular food effectively. In this respect the allergenicity of food fractions, particularly the alcohols, sugars, starches, proteins and fats of particular foods, should be considered. The detail of this information is of such a magnitude that a clinician interested in this work should be in a position to instruct his patients in these minutiae by means of readily available written forms designed for this purpose.

In summary, there is no short cut to the specific diagnosis of food allergy. The number of possible etiologic factors involved and the variations in the eating habits of different individuals necessitate an individualized approach to this problem although some standardization of certain aspects of this work is permissible.

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THE MANAGEMENT OF FOOD ALLERGY

HERBERT J. RINKEL, M.D.
KANSAS CITY, MO.

THE management of food allergy consists of two problems: first, the immediate one which is to relieve the patient of allergic symptoms and, second, the delayed one which involves (a) the administration of prophylactic measures, (b) the diagnosis of newly developing sensitizations, (c) the seasonal factors, (d) the handling of previously allergenic foods to which the patient has gained tolerance by strict elimination of these foods. It also includes drug therapy and the mineral as well as the vitamin needs.

PREREQUISITES TO THE MANAGEMENT OF FOOD ALLERGY

The first prerequisite, and an exceedingly important one, is the adequate control of inhalant allergy, except in those instances in which inhalants are not a factor. One should not discount the importance of inhalant allergy in patients with migraine although it is not a frequent factor. There are patients with gastrointestinal symptoms who have exacerbations due to contacts with specific inhalants. The insistence that there be adequate control of the inhalants before proceeding with food management is not based upon any apology for the clinical importance of food allergy but, rather, upon the fact that there are certain instances in which the food may be tolerated providing the patient is adequately protected from the inhalants. Furthermore, when one uses the occurrence of symptoms as a diagnostic measure it is imperative that there be no exacerbations due to inhalants. This could easily be true if the patient was not adequately controlled for his inhalant sensitizations. "Adequate control" is a phrase which implies a great deal of highly detailed technical work. It means not only that patients have been tested with those inhalants which might be considered important but that they are tested for all the inhalants which are contacted during the period of occurrence of symptoms. Furthermore, this testing will involve the establishment not only of the presence of each sensitivity but also of its relative degree. In this therapeutic program one should give adequate and detailed attention to determining the correct and exact amount of antigen which will give the patient the greatest degree of relief. It is possible, in certain instances, for one to pass through the zone of effective relief of therapeutic solutions without being aware of it when using the regular increment of doses which has proved satisfactory for the great majority of the patients.

The second prerequisite to the management of food allergy is a clinical knowledge of food allergy. Among other things, this includes a knowledge of the interval between ingestion and the onset of symptoms. In a series of 376 patients who were symptom free at the time they were fed foods which had been avoided four days, 84 per cent developed symptoms within 28 minutes after eating the food. The earliest evidence of reaction occurred within three minutes, and the greatest number of patients to evidence symptoms at any one time was 27 at ten minutes after the start of the ingestion of the food. The latest occurrence of symptoms we have been able to prove beyond a possible doubt took place 13 hours after ingestion. The duration of symptoms will vary from a few hours to a maximum of five days. Even in those cases where physical collapse has followed the ingestion of a food under test conditions (a condition which has only occurred a half dozen times in 30,000 tests),[5] the patient was entirely free of symptoms 72 hours after the ingestion of the food. Symptoms may continue for at least five days in patients with perennial nasal allergy and asthma, particularly in the winter, following the eating of specific foods and subsequent chilling. The purulent secretions which occur with these reactions are the sequelae of the allergic episode.

The third important clinical factor in food allergy is a knowledge of the sequelae to reactions. One has just been mentioned, that is, the development of purulent secretions which will prolong the duration of symptoms following the specific ingestion from approximately 72 hours to a maximum of five days when the etiologic factor has been contacted but once. There are, however, instances in which patients will eat a known allergenic food a single time and have symptoms continue for two or three weeks. One of the reasons for the apparent inconsistency is that, following some acute allergic exacerbations, one may temporarily destroy the perfect masking of some other food. To illustrate this, on one of our experiments in

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the production of an acute "cold" it was observed on one occasion that the reaction did not cease at the end of five days as was expected. It did not clear until 72 hours following the elimination of a food which had caused the same type of reaction several years previous. This food had been re-introduced into the diet after a year's omission and tolerance was finally built up to its use once daily. It was suspected on the eighteenth day of symptoms that this food for which the patient had a perfect masking might be the cause of trouble. It was eliminated and symptoms cleared in three days.

There is another condition which may cause a prolonged reaction. Sometimes when a patient eats an allergenic food the symptoms do not subside as expected. It has been found in a number of these cases that these acute reactions destroy one's tolerance for closely related foods or for foods barely tolerated. One of the most valid arguments for not breaking the diet is the fact that on a good number of occasions the patient creates new allergies.

THE IMMEDIATE PROBLEM IN THE MANAGEMENT OF PATIENTS WITH FOOD ALLERGY

Foods Which Must Be Eliminated Entirely and Consistently

This group of foods will be considered under two headings: (1) the foods which are complex in form and usage and (2) those which are used in their primary forms without fractionation or processing refinements.

The Complex Foods. The most common foods which may be used in many forms and in processed portions are wheat, eggs, milk, corn, soybeans and cottonseed. One might well include peanuts; however, the first six named have been of the greatest importance. When patients are required to eliminate these foods, it is necessary to give them printed instructions concerning the sources of possible contacts. It is sheer folly to ask a patient to eliminate complex foods without specific information concerning contacts. The patient has no means of knowing these unless they have been specifically informed of these various sources. Unless education of the patient is carried out in a purposeful, aggressive manner by the physician, the patient will continue to have symptoms in spite of the fact that all of the allergenic foods are diagnosed. One frequently sees patients who are known to be sensitive to one or more of these complex foods who have not become free of symptoms with their supposed elimination. Many of these have been relieved promptly after being given printed information concerning contacts and have remained so except for the inevitable, occasional, accidental ingestion of these foods.

The Primary Foods. The second group of foods to be avoided completely are those used in primary forms (such as asparagus, carrots, and string beans). There is usually little difficulty in teaching patients to localize contacts with such foods and their elimination calls for no special programmatic study.

Foods Which Need Not Be Eliminated Entirely

There are a number of foods which do not need to be avoided entirely and these should be retained in the diet when one is certain that this intermittent or fractionated usage is not followed by symptoms. This subject is divided into two phases, (1) that of interval usage and (2) that of fractionated portions of edible foods which are tolerated.

Foods Tolerated at Intervals. If one will go to the trouble to ascertain this fact, he will find that there are a number of foods which patients can eat at intervals but these foods cannot be taken daily. Again, there are foods which can only be used once daily every other day, or every third day, et cetera. The interval of usage must be determined for each food after the patient has become symptom free, that is, the keystone of diagnosis has been accomplished. This may be said to exist when the patient is consistently controlled on a known diet and with adequate inhalant therapy. The evaluation of foods which may be eaten at intervals calls for particular attention to early toxic symptoms, fatigue and excessive perspiration, as well as to the delayed reactions. The most common delayed manifestation is acute exacerbations during the night and upon arising.

Foods Tolerated in Processed Fractions. The second group of foods which need not be avoided entirely and consistently is comprised of those which can be used in fractionated portions. Examples from this group will include corn sugar, corn starch, corn oil, cottonseed oil and soybean oil. There are patients who can eat roasting ears with impunity but cannot take any ripe corn products without having symptoms. Again, green beans may be tolerated but ripe ones may cause a reaction. Very often cooked fruits are permissible when the raw ones produce symptoms. In all instances when a fraction of a food, or a form of a food, proves agreeable and the whole product does not the patient should be restricted in the use of the tolerated fraction or form. It is best to feed these tolerated materials at intervals of once in three days. The physician should keep in mind that the variation in effect of these processed or fractionated forms of the same food is only a relative and not an absolute difference in sen-

sitivity. It is the clinically acceptable procedure to eliminate entirely a reacting food, including all fractions, until the patient has been controlled. Then one should determine which, if any, of these processed fractions are tolerated and at what interval they may be used.

Geographic Factors in Dietary Restrictions

Patients who live in one area of the country do not necessarily have to eliminate all the foods to which they are sensitive when they go to a different area. The most common example of this is the patient whose respiratory allergy recurs when he returns to Kansas City from a Colorado vacation. A great number of these patients report a recurrence of symptoms when they are approximately one-third of the way through Kansas. It has been found that if these patients are placed on their diets three days before starting back home, they are able to cross Kansas without a recurrence of symptoms. This type of reaction is based upon a concomitant sensitization between a food and a specific inhalant. Should these patients decide to reside in the area where they are now temporarily free of symptoms, this phenomenon disappears since, almost without exception, they acquire new sensitizations.

There may be other factors involved in reactions apparently due to geographic influences. Rackemann[2] has reported a patient who could eat potatoes from Maine but not those from Rhode Island. It was discovered that this was due to a mold peculiar to the Rhode Island potatoes. There has been a report that certain patients could eat California cantaloupes but could not tolerate those from Colorado. A study of the occurrence of symptoms and the season of usage will reveal that when the patient ceases to use Colorado cantaloupes he has about ten months time to develop tolerance to cantaloupe before the next season of the California melons. Therefore, he can use them without symptoms for a while (cyclic type of sensitivity[4]). However, a degree of sensitivity is built up and in the interval between the California and Colorado seasons his reaction is unmasked. Then with the first feeding of the Colorado melon the patient has a reaction. Actually the patient would have symptoms from cantaloupe produced in either area *providing* they were eaten under the same conditions. This type of response to foods indicates the importance of a knowledge of the dynamic nature of food allergy.

THE DELAYED PROBLEM IN THE MANAGEMENT OF PATIENTS WITH FOOD ALLERGY

Prophylactic Measures

One of the important therapeutic procedures which can be used for the benefit of the patient is a program to prevent development of new food allergies. In light of our present knowledge, there is no procedure which is more satisfactory than that of the rotation and the diversification of the diet.[6] One can state the basic nature of the diet in this manner: It consists in the usage of various tolerated foods once daily at specific intervals, usually once daily every third day. In some instances it is possible to use a food once daily every other day. All portions and fractions of the food used are rotated in unison. In other words, if one is rotating grapes, he must not only rotate grapes as a fruit but grape jam, grape jelly, grape by-products including wines, champagne and rums (since sherry wine is included in practically all rums[3]).

The Development of New Sensitizations

If one will visualize the development of food allergy as being similar to a horse race (the horses across the finish line being comparable to those allergens precipitating symptoms), he will better understand this delayed problem with regular usage. When no specific measures are taken to prevent the continuing development of new sensitizations, it is to be expected that some patients will develop new food allergies from time to time. This will depend upon (1) the frequency of use, (2) the amount of the specific foods taken and (3) the inherent tolerance of the patient.[4] Some patients sensitize much easier than others. In our experience the only procedure that has been helpful in avoiding these new sensitizations is the diversification of the diet as much as possible and the reduction of their frequency as early in therapy as can be done with safety.

The Use of Foods for Which Tolerance Has Been Acquired

This is usually the result of deliberate and long continued absolute elimination of specific foods diagnosed earlier in the period of study. We have found it practical to make the first test for tolerance after six months of elimination. If the patient again reacts to the food, subsequent tests are spaced at three month intervals. At whatever time following the original elimination the food can be taken under test conditions without provoking a reaction, it is admitted to the diet once daily every fifth day for six feedings. The object of this is to avoid masking and to produce clear-cut post-meal reactions if symptoms should occur. If, after the six feedings, the food is still tolerated, one should shorten the interval from five to three days and continue the food once daily every third day for at least three months before attempting to use it at shorter intervals. Experience has shown that it is not

highly desirable to use any previously allergenic food (even though it is tolerated following omission) at intervals of less than once in three days although *necessity* should dictate the shortest interval.

The Factor of Seasonal Changes

Some food allergies are perennial but others are not. Some may be concomitant only. Thus, a patient may be controlled during June and yet it would not be unusual to find that he begins to have difficulty due to specific foods around the fourteenth of July (pigweed), again around the twenty-fourth of July (kochia), or about the tenth, twentieth, or twenty-fifth of August (ragweed), as these are the seasons that specific inhalant factors may initiate concomitant reactions.

The Factor of Thermal Changes

The thermal type of food allergy refers to those foods whose symptomatic response occurs with, or is increased with, the breathing of cool air or with chilling. These foods may also increase the patient's susceptibility to changes in temperature. Note that there are *two factors*: (1) an increased production of symptoms and (2) a lessening of the patient's ability to withstand changes in temperature. Because of this second factor the patient will tend to protect himself, and in extreme cases, this protection of oneself from changes in temperature will lead to a greatly increased sensitivity to such temperature changes until the patient may not be able to get out of bed and dress without feeling ill. This was originally emphasized by Duke.[1] It is also possible in patients with the thermal type of allergy (when they have lost their ability to withstand ordinary temperature changes) to have a continuation of symptoms longer than five days. I have seen a patient continue to have purulent expectorations, afternoon temperature, and marked sensitivity to thermal changes for three weeks after ingestion of a specific food. Symptoms did not abate until therapeutic measures were instituted to neutralize this excessive sensitivity to temperature changes. Such procedures consisted in the use of alternate hot and cold showers, or the use of ice rubs, and exposure to heat. This program may be enhanced by small doses of histamine.[7] It is imperative to note that the ingestion of a specific food may institute a chain of symptoms which are prolonged beyond the period of the usual response to foods. When such patients have rebuilt their ability to withstand ordinary changes in temperature, the subsequent ingestion of these foods will not produce reactions lasting over a five-day period.

Escalator Additions

In the course of handling all patients with food allergies, it becomes necessary from time to time to increase the diet from the so-called basic diet (this may be one of several diets, either derived from individual feeding tests, an asymptomatic period, or a prescribed diet based on history and personal observations). In the course of making these additions it is necessary to consider them under two headings.

First, foods which have not been omitted for more than ten days. In adding such foods to the diet it is satisfactory if the food is fed at the noon meal and repeated in the middle of the afternoon. Or, if this is not convenient, with the evening meal. If no symptoms are precipitated following either feeding and there is no flare during the night or upon arising, the food is returned to the diet and used *with the same frequency as it was before omission and addition.*

The second group of foods are those which have been avoided for longer than ten days. It has been shown[5] that a patient may gain enough tolerance to be able to eat a food once without difficulty when the food has been eliminated only twelve days. Therefore, foods which have been avoided longer than ten days should be used twice daily for at least two successive days. As the period of omission increases, the usage may well be twice daily for two, three or even four days, before the food is returned for regular use. However, if the patient wishes to use this food only once daily every third or fourth day, the two feedings in one day should be sufficient. Whenever a food is fed two and three times daily for two weeks before symptoms occur, one is not discovering an allergy. He is creating one, and this is not a satisfactory clinical procedure from the patient's standpoint. Therefore, in making escalator additions one should determine the type of test procedure by the desired subsequent frequency of usage.

Drugs

The drugs which have been found to be of the greatest value in the handling of acute food allergy reactions, irrespective of whether they are accidental or deliberately induced, have been few. It has proved of value in a great number of instances to give a saline or other brisk cathartic immediately following the ingestion of a specific allergen. However, one should be certain he is dealing with a food reaction and not the early stages of an infectious process.

We have found that the most satisfactory drug is the combination of one of the antihistaminic drugs with aminophylline and syn-

thetic or natural ephedrine. All too often ephedrine produces adverse reactions, particularly in elderly men, so we prefer the combinations mentioned rather than ephedrine and some barbituric acid preparation.

Vaughan[8] pointed out years ago that if one wishes to use adrenalin in an acute gastrointestinal reaction, the patient must be kept in a state of pallor and tremor over a considerable period of time in order to abort the attack. Obviously the use of adrenalin is highly desirable in patients who have asthmatic reactions from specific food allergens.

We have not found the antihistaminics alone to be of sufficient value to recommend them. There are instances in which the use of sublingual medication is highly desirable if one cannot use hypodermic injections. This is due to the fact that all too often capsules or tablets taken orally in the presence of food reactions are not absorbed rapidly.

The importance of an adequate intake of vitamin B complex as well as vitamins C and D should be stressed. If one uses rotation and a diversified diet, his needs for accessory vitamin medication will not be as great as if strict and absolute elimination and a narrowed diet are used. In conjunction with the use of vitamin B complex, it has been my experience that a number of these products cause symptoms and one may have to try B complex from various sources. The B complex may be obtained from beef, pork, or brewers' yeast as well as from rye (Burroughs-Welcome). There are also a number of products which are primarily synthetic. One may be able to administer vitamin B complex at intervals in cases when it is not tolerated daily.

SUMMARY AND CONCLUSION

1. The management of patients with food allergy is a program which necessitates a considerable period of time and care. The evaluation of a number of factors cannot be completed at the time the patient is originally tested and freed of symptoms.

2. It is important that the patient be made aware of the necessity of this long continued, exacting program. He should not expect to become free of symptoms immediately and continuously by the mere fact that tests have revealed one or more allergenic foods.

3. Printed instructions are invariably required concerning contacts with wheat, corn, eggs, milk, soybeans and cottonseed. These are to be supplemented by personal instructions.

4. The delayed features in management include not only the development of new sensitizations but the handling of foods for which the patient gained tolerance by omission and, finally, prophylactic measures to prevent new allergies.

5. Drugs, vitamin and mineral therapy are a part of the therapeutic program in all cases and should be thoroughly evaluated.

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